

SEQUENCE LISTING

<110> Mosley, Ralph T.
 McKeever, Brian Michael
 Berger, Joel P.

<120> PEROXISOME PROLIFERATOR-ACTIVATED
 RECEPTOR

<130> 21269P

<150> PCT/US2004/001221

<151> 2004-01-16

<150> 60/441,836

<151> 2003-01-22

<160> 12

<170> FastSEQ for Windows Version 4.0

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<211> 468

<212> PRT

<213> Human

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Phe	Gly	Phe	Thr	Glu	Tyr	Gln	Tyr	Leu	Gly	Ser	Cys	Pro	Gly	Ser	Asp
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Gly	Ser	Val	Ile	Thr	Asp	Thr	Leu	Ser	Pro	Ala	Ser	Ser	Pro	Ser	Ser
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Val	Thr	Tyr	Pro	Val	Val	Pro	Gly	Ser	Val	Asp	Glu	Ser	Pro	Ser	Gly
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145				150					155					160	
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Pro	Arg	Ser	Glu	Lys	Ala	Lys	Leu	Lys	Ala	Glu	Ile	Leu	Thr	Cys	Glu
			180					185				190			
His	Asp	Ile	Glu	Asp	Ser	Glu	Thr	Ala	Asp	Leu	Lys	Ser	Leu	Ala	Lys
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Arg	Ile	Tyr	Glu	Ala	Tyr	Leu	Lys	Asn	Phe	Asn	Met	Asn	Lys	Val	Lys
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Ala Arg Val Ile Leu Ser Gly Lys Ala Ser Asn Asn Pro Pro Phe Val
 225 230 235 240
 Ile His Asp Met Glu Thr Leu Cys Met Ala Glu Lys Thr Leu Val Ala
 245 250 255
 Lys Leu Val Ala Asn Gly Ile Gln Asn Lys Glu Ala Glu Val Arg Ile
 260 265 270
 Phe His Cys Cys Gln Cys Thr Ser Val Glu Thr Val Thr Glu Leu Thr
 275 280 285
 Glu Phe Ala Lys Ala Ile Pro Gly Phe Ala Asn Leu Asp Leu Asn Asp
 290 295 300
 Gln Val Thr Leu Leu Lys Tyr Gly Val Tyr Glu Ala Ile Phe Ala Met
 305 310 315 320
 Leu Ser Ser Val Met Asn Lys Asp Gly Met Leu Val Ala Tyr Gly Asn
 325 330 335
 Gly Phe Ile Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Cys
 340 345 350
 Asp Ile Met Glu Pro Lys Phe Asp Phe Ala Met Lys Phe Asn Ala Leu
 355 360 365
 Glu Leu Asp Asp Ser Asp Ile Ser Leu Phe Val Ala Ala Ile Ile Cys
 370 375 380
 Cys Gly Asp Arg Pro Gly Leu Leu Asn Val Gly His Ile Glu Lys Met
 385 390 395 400
 Gln Glu Gly Ile Val His Val Leu Arg Leu His Leu Gln Ser Asn His
 405 410 415
 Pro Asp Asp Ile Phe Leu Phe Pro Lys Leu Leu Gln Lys Met Ala Asp
 420 425 430
 Leu Arg Gln Leu Val Thr Glu His Ala Gln Leu Val Gln Ile Ile Lys
 435 440 445
 Lys Thr Glu Ser Asp Ala Ala Leu His Pro Leu Leu Gln Glu Ile Tyr
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 Arg Asp Met Tyr
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 35 40 45
 Ser Ser Pro Pro Ser Leu Leu Asp Gln Leu Gln Met Gly Cys Asp Gly
 50 55 60
 Ala Ser Cys Gly Ser Leu Asn Met Glu Cys Arg Val Cys Gly Asp Lys
 65 70 75 80
 Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly
 85 90 95
 Phe Phe Arg Arg Thr Ile Arg Met Lys Leu Glu Tyr Glu Lys Cys Glu
 100 105 110

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Phe	Gly	Arg	Met	Pro	Glu	Ala	Glu	Lys	Arg	Lys	Leu	Val	Ala	Gly	Leu
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Thr	Ala	Asn	Glu	Gly	Ser	Gln	Tyr	Asn	Pro	Gln	Val	Ala	Asp	Leu	Lys
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Ala	Phe	Ser	Lys	His	Ile	Tyr	Asn	Ala	Tyr	Leu	Lys	Asn	Phe	Asn	Met
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Thr	Lys	Lys	Lys	Ala	Arg	Ser	Ile	Leu	Thr	Gly	Lys	Ala	Ser	His	Thr
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Ile	Ser	Val	His	Val	Phe	Tyr	Arg	Cys	Gln	Cys	Thr	Thr	Val	Glu	Thr
				245					250					255	
Val	Arg	Glu	Leu	Thr	Glu	Phe	Ala	Lys	Ser	Ile	Pro	Ser	Phe	Ser	Ser
			260					265					270		
Leu	Phe	Leu	Asn	Asp	Gln	Val	Thr	Leu	Leu	Lys	Tyr	Gly	Val	His	Glu
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Ala	Ile	Phe	Ala	Met	Leu	Ala	Ser	Ile	Val	Asn	Lys	Asp	Gly	Leu	Leu
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Val	Ala	Asn	Gly	Ser	Gly	Phe	Val	Thr	Arg	Glu	Phe	Leu	Arg	Ser	Leu
305					310					315					320
Arg	Lys	Pro	Phe	Ser	Asp	Ile	Ile	Glu	Pro	Lys	Phe	Glu	Phe	Ala	Val
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Lys	Phe	Asn	Ala	Leu	Glu	Leu	Asp	Asp	Ser	Asp	Leu	Ala	Leu	Phe	Ile
			340					345					350		
Ala	Ala	Ile	Ile	Leu	Cys	Gly	Asp	Arg	Pro	Gly	Leu	Met	Asn	Val	Pro
		355					360					365			
Arg	Val	Glu	Ala	Ile	Gln	Asp	Thr	Ile	Leu	Arg	Ala	Leu	Glu	Phe	His
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Leu	Gln	Ala	Asn	His	Pro	Asp	Ala	Gln	Tyr	Leu	Phe	Pro	Lys	Leu	Leu
385					390					395					400
Gln	Lys	Met	Ala	Asp	Leu	Arg	Gln	Leu	Val	Thr	Glu	His	Ala	Gln	Met
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Met	Gln	Arg	Ile	Lys	Lys	Thr	Glu	Thr	Glu	Thr	Ser	Leu	His	Pro	Leu
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<211> 477

<212> PRT

<213> Human

<400> 3

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			20					25					30		

Asp	Ile	Lys	Pro	Phe	Thr	Thr	Val	Asp	Phe	Ser	Ser	Ile	Ser	Thr	Pro	35	40	45
His	Tyr	Glu	Asp	Ile	Pro	Phe	Thr	Arg	Thr	Asp	Pro	Val	Val	Ala	Asp	50	55	60
Tyr	Lys	Tyr	Asp	Leu	Lys	Leu	Gln	Glu	Tyr	Gln	Ser	Ala	Ile	Lys	Val	65	70	75
Glu	Pro	Ala	Ser	Pro	Pro	Tyr	Tyr	Ser	Glu	Lys	Thr	Gln	Leu	Tyr	Asn	85	90	95
Lys	Pro	His	Glu	Glu	Pro	Ser	Asn	Ser	Leu	Met	Ala	Ile	Glu	Cys	Arg	100	105	110
Val	Cys	Gly	Asp	Lys	Ala	Ser	Gly	Phe	His	Tyr	Gly	Val	His	Ala	Cys	115	120	125
Glu	Gly	Cys	Lys	Gly	Phe	Phe	Arg	Arg	Thr	Ile	Arg	Leu	Lys	Leu	Ile	130	135	140
Tyr	Asp	Arg	Cys	Asp	Leu	Asn	Cys	Arg	Ile	His	Lys	Lys	Ser	Arg	Asn	145	150	155
Lys	Cys	Gln	Tyr	Cys	Arg	Phe	Gln	Lys	Cys	Leu	Ala	Val	Gly	Met	Ser	165	170	175
His	Asn	Ala	Ile	Arg	Phe	Gly	Arg	Met	Pro	Gln	Ala	Glu	Lys	Glu	Lys	180	185	190
Leu	Leu	Ala	Glu	Ile	Ser	Ser	Asp	Ile	Asp	Gln	Leu	Asn	Pro	Glu	Ser	195	200	205
Ala	Asp	Leu	Arg	Ala	Leu	Ala	Lys	His	Leu	Tyr	Asp	Ser	Tyr	Ile	Lys	210	215	220
Ser	Phe	Pro	Leu	Thr	Lys	Ala	Lys	Ala	Arg	Ala	Ile	Leu	Thr	Gly	Lys	225	230	235
Thr	Thr	Asp	Lys	Ser	Pro	Phe	Val	Ile	Tyr	Asp	Met	Asn	Ser	Leu	Met	245	250	255
Met	Gly	Glu	Asp	Lys	Ile	Lys	Phe	Lys	His	Ile	Thr	Pro	Leu	Gln	Glu	260	265	270
Gln	Ser	Lys	Glu	Val	Ala	Ile	Arg	Ile	Phe	Gln	Gly	Cys	Gln	Phe	Arg	275	280	285
Ser	Val	Glu	Ala	Val	Gln	Glu	Ile	Thr	Glu	Tyr	Ala	Lys	Ser	Ile	Pro	290	295	300
Gly	Phe	Val	Asn	Leu	Asp	Leu	Asn	Asp	Gln	Val	Thr	Leu	Leu	Lys	Tyr	305	310	315
Gly	Val	His	Glu	Ile	Tyr	Thr	Met	Leu	Ala	Ser	Leu	Met	Asn	Lys		325	330	335
Asp	Gly	Val	Leu	Ile	Ser	Glu	Gly	Gln	Gly	Phe	Met	Thr	Arg	Glu	Phe	340	345	350
Leu	Lys	Ser	Leu	Arg	Lys	Pro	Phe	Gly	Asp	Phe	Met	Glu	Pro	Lys	Phe	355	360	365
Glu	Phe	Ala	Val	Lys	Phe	Asn	Ala	Leu	Glu	Leu	Asp	Asp	Ser	Asp	Leu	370	375	380
Ala	Ile	Phe	Ile	Ala	Val	Ile	Ile	Leu	Ser	Gly	Asp	Arg	Pro	Gly	Leu	385	390	395
Leu	Asn	Val	Lys	Pro	Ile	Glu	Asp	Ile	Gln	Asp	Asn	Leu	Leu	Gln	Ala	405	410	415
Leu	Glu	Leu	Gln	Leu	Lys	Leu	Asn	His	Pro	Glu	Ser	Ser	Gln	Leu	Phe	420	425	430
Ala	Lys	Leu	Leu	Gln	Lys	Met	Thr	Asp	Leu	Arg	Gln	Ile	Val	Thr	Glu	435	440	445
His	Val	Gln	Leu	Leu	Gln	Val	Ile	Lys	Lys	Thr	Glu	Thr	Asp	Met	Ser	450	455	460

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<210> 4

<211> 275

<212> PRT

<213> Artificial Sequence

<220>

<223> mutated PPAR ligand binding domain

<221> VARIANT

<222> 271

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 proline, tryptophan, phenylalanine, methionine,
 histidine, asparagine, or glutamine

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			20					25					30		
Ala	Ile	Leu	Thr	Gly	Lys	Thr	Thr	Asp	Lys	Ser	Pro	Phe	Val	Ile	Tyr
		35					40					45			
Asp	Met	Asn	Ser	Leu	Met	Met	Gly	Glu	Asp	Lys	Ile	Lys	Phe	Lys	His
	50					55					60				
Ile	Thr	Pro	Leu	Gln	Glu	Gln	Ser	Lys	Glu	Val	Ala	Ile	Arg	Ile	Phe
65					70					75				80	
Gln	Gly	Cys	Gln	Phe	Arg	Ser	Val	Glu	Ala	Val	Gln	Glu	Ile	Thr	Glu
				85					90					95	
Tyr	Ala	Lys	Ser	Ile	Pro	Gly	Phe	Val	Asn	Leu	Asp	Leu	Asn	Asp	Gln
			100					105					110		
Val	Thr	Leu	Leu	Lys	Tyr	Gly	Val	His	Glu	Ile	Ile	Tyr	Thr	Met	Leu
			115				120					125			
Ala	Ser	Leu	Met	Asn	Lys	Asp	Gly	Val	Leu	Ile	Ser	Glu	Gly	Gln	Gly
	130					135					140				
Phe	Met	Thr	Arg	Glu	Phe	Leu	Lys	Ser	Leu	Arg	Lys	Pro	Phe	Gly	Asp
145					150					155					160
Phe	Met	Glu	Pro	Lys	Phe	Glu	Phe	Ala	Val	Lys	Phe	Asn	Ala	Leu	Glu
				165				170						175	
Leu	Asp	Asp	Ser	Asp	Leu	Ala	Ile	Phe	Ile	Ala	Val	Ile	Ile	Leu	Ser
			180					185					190		
Gly	Asp	Arg	Pro	Gly	Leu	Leu	Asn	Val	Lys	Pro	Ile	Glu	Asp	Ile	Gln
	195						200					205			
Asp	Asn	Leu	Leu	Gln	Ala	Leu	Glu	Leu	Gln	Leu	Lys	Leu	Asn	His	Pro
	210					215					220				
Glu	Ser	Ser	Gln	Leu	Phe	Ala	Lys	Leu	Leu	Gln	Lys	Met	Thr	Asp	Leu
225					230					235					240
Arg	Gln	Ile	Val	Thr	Glu	His	Val	Gln	Leu	Leu	Gln	Val	Ile	Lys	Lys
				245				250						255	
Thr	Glu	Thr	Asp	Met	Ser	Leu	His	Pro	Leu	Leu	Gln	Glu	Ile	Xaa	Lys
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Asp	Leu	Tyr													
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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> transcription factor containing a mutated PPAR
 ligand binding domain

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 35 40 45
 Leu Thr Arg Ala His Leu Thr Glu Val Glu Ser Arg Leu Glu Arg Leu
 50 55 60
 Glu Gln Leu Phe Leu Leu Ile Phe Pro Arg Glu Asp Leu Asp Met Ile
 65 70 75 80
 Leu Lys Met Asp Ser Leu Gln Asp Ile Lys Ala Leu Leu Thr Gly Leu
 85 90 95
 Phe Val Gln Asp Asn Val Asn Lys Asp Ala Val Thr Asp Arg Leu Ala
 100 105 110
 Ser Val Glu Thr Asp Met Pro Leu Thr Leu Arg Gln His Arg Ile Ser
 115 120 125
 Ala Thr Ser Ser Ser Glu Glu Ser Ser Asn Lys Gly Gln Arg Gln Leu
 130 135 140
 Thr Val Ser Pro Gly Ile Arg Met Ser His Asn Ala Ile Arg Phe Gly
 145 150 155 160
 Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu Ala Glu Ile Ser Ser
 165 170 175
 Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp Leu Arg Ala Leu Ala
 180 185 190
 Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala
 195 200 205
 Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe
 210 215 220
 Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys
 225 230 235 240
 Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile
 245 250 255
 Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu
 260 265 270
 Ile Thr Glu Tyr Ala Lys Ser Ile Pro Gly Phe Val Asn Leu Asp Leu
 275 280 285
 Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr
 290 295 300
 Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu
 305 310 315 320
 Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro
 325 330 335

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Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn
      340      345      350
Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile
      355      360      365
Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu
      370      375      380
Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu
      385      390      395      400
Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met
      405      410      415
Thr Asp Leu Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val
      420      425      430
Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu
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Ile Ala Lys Asp Leu Tyr
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<210> 6

<211> 454

<212> PRT

<213> Artificial Sequence

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<223> transcription factor containing a mutated PPAR
      ligand binding domain

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<400> 6

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      20      25      30
Lys Asn Asn Trp Glu Cys Arg Tyr Ser Pro Lys Thr Lys Arg Ser Pro
      35      40      45
Leu Thr Arg Ala His Leu Thr Glu Val Glu Ser Arg Leu Glu Arg Leu
      50      55      60
Glu Gln Leu Phe Leu Leu Ile Phe Pro Arg Glu Asp Leu Asp Met Ile
      65      70      75      80
Leu Lys Met Asp Ser Leu Gln Asp Ile Lys Ala Leu Leu Thr Gly Leu
      85      90      95
Phe Val Gln Asp Asn Val Asn Lys Asp Ala Val Thr Asp Arg Leu Ala
      100      105      110
Ser Val Glu Thr Asp Met Pro Leu Thr Leu Arg Gln His Arg Ile Ser
      115      120      125
Ala Thr Ser Ser Ser Glu Glu Ser Ser Asn Lys Gly Gln Arg Gln Leu
      130      135      140
Thr Val Ser Pro Gly Ile Arg Met Ser His Asn Ala Ile Arg Phe Gly
      145      150      155      160
Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu Ala Glu Ile Ser Ser
      165      170      175
Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp Leu Arg Ala Leu Ala
      180      185      190
Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala
      195      200      205
Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe
      210      215      220

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Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys
225                230                235                240
Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile
                245                250                255
Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu
                260                265                270
Ile Thr Glu Tyr Ala Lys Ser Ile Pro Gly Phe Val Asn Leu Asp Leu
                275                280                285
Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr
                290                295                300
Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu
305                310                315                320
Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro
                325                330                335
Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn
                340                345                350
Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile
                355                360                365
Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu
370                375                380
Asp Ile Gln Asp Asn Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu
385                390                395                400
Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met
                405                410                415
Thr Asp Leu Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val
                420                425                430
Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu
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Ile Phe Lys Asp Leu Tyr
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<210> 7

<211> 1365

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence encoding GAL4/PPARγ (473
Ala)

<400> 7

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tctcccaaaa caaaagggtc tccgctgact agggcacatc tgacagaagt ggaatcaagg 180
ctagaaagac tggaacagct atttctactg atttttcctc gagaagacct tgacatgatt 240
ttgaaaatgg attctttaca ggatataaaa gcattgttaa caggattatt tgtacaagat 300
aatgtgaata aagatgccgt cacagataga ttggcttcag tggagactga tatgcctcta 360
acattgagac agcatagaat aagtgcgaca tcatcatcgg aagagagtag taacaaagg 420
caaagacagt tgactgtatc gccggggatc cggatgtctc ataatgccat caggtttggg 480
cggatgccac aggccgagaa ggagaagctg ttggcggaga tctccagtga tatcgaccag 540
ctgaatccag agtccgctga cctccgggcc ctggcaaaac atttgtatga ctcatacata 600
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aaatcaccat tcgttatcta tgacatgaat tccttaatga tgggagaaga taaaatcaag 720
ttcaaacaca tccccccct gcaggagcag agcaaagagg tggccatccg catctttcag 780
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ggccaaggct tcatgacaag ggagtttcta aagagcctgc gaaagccttt tggtgacttt 1020
atgggagccca agtttgagtt tgctgtgaag ttcaatgcac tgggaattaga tgacagcgac 1080
ttggcaatat ttattgctgt cattattctc agtggagacc gcccagggttt gctgaatgtg 1140
aagcccattg aagacattca agacaacctg ctacaagccc tggagctcca gctgaagctg 1200
aaccaccctg agtcctcaca gctgtttgcc aagctgctcc agaaaatgac agacctcaga 1260
cagattgtca cggaacacgt gcagctactg caggatgatca agaagacgga gacagacatg 1320
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<210> 8

<211> 1365

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence encoding GAL4/PPARγ (473 Phe)

<400> 8

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tctcccaaaa ccaaaaggct tccgctgact agggcacatc tgacagaagt ggaatcaagg 180
ctagaaagac tggaacagct atttctactg atttttcttc gagaagacct tgacatgatt 240
ttgaaaatgg attctttaca ggatataaaa gcattgttaa caggattatt tgtacaagat 300
aatgtgaata aagatgccgt cacagataga ttggcttcag tggagactga tatgcctcta 360
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